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TRANS-ATLANTIC DEBATE

Thomas L. Forbes, MD, and Jean-Baptiste Ricco, MD, PhD, Section Editors

Role of interventions for atherosclerotic renal artery stenoses

Vikram S. Kashyap, MD,[a] **Fabrice Schneider, MD,**[b] and **Jean-Baptiste Ricco, MD, PhD,**[b] *Cleveland, Ohio; and Poitiers, France*

The role of and indications for interventions for renal artery stenosis have long been a hot topic of debate. Despite numerous reports and studies over the years, there remain many unanswered questions. Among them are: Who should be intervened upon? What should be the objectives of intervention? What is the optimal mode of intervention? More recently, several randomized studies have attempted to answer some of these basic questions, but unfortunately have left many unanswered questions. In the following debate, the authors consider the existing literature and attempt to convince us that the majority, or the minority, of patients with renal artery stenoses should be intervened upon. (J Vasc Surg 2011;54:563-70.)

PART I: THE VAST MAJORITY OF PATIENTS WITH RENAL ARTERY STENOSES REQUIRE INTERVENTION

Vikram S. Kashyap, MD, *Cleveland, Ohio*

Introduction. The debate position given to this author may on first glance seem to be untenable. I hope to convince you that the opposite stance of not treating patients with renal artery stenosis (RAS) neglects the opportunity to help some patients with correctable hypertension and renal dysfunction. Frankly, either debate position is difficult to defend given our dearth of solid information in the arena of renovascular disease. As a medical community, we have scant evidence on the natural history of RAS and the kidneys these arteries are supplying. Furthermore, the available data are far from convincing especially given the flawed trial designs in most of the prospective trials. Clearly, further study on renovascular disease may lead us to better medical management, patient selection for intervention, and technical success in those patients that are intervened upon. I do not believe a global position of benign neglect of renal artery disease will be in the best interest of patients with this morbid condition. There are some current posits that require re-examination. The following widely held myths need scrutiny.

Myth #1. Atherosclerosis in the renal arteries is benign. In every arterial bed, the severe consequences of arterial narrowing secondary to atherosclerosis are recognized. The initiation and progression of atherogenesis, plaque rupture, thrombosis, embolization, dissection, and resultant end-organ deterioration is well delineated in arterial beds from the skull to the toe. For instance, the process of discovery that extracranial cerebrovascular disease caused artery-to-artery embolization leading to stroke took decades.[1] Furthermore, treatment of the offending lesion to prevent further stroke and death required rigorous randomized controlled trials first in symptomatic patients.[2] Surgical treatment in the form of endarterectomy removes the plaque leading to embolization and was found better than medical therapy in the long-term stroke-free survival of asymptomatic patients[3] in the largest surgical trial to date.[4] The limb and life-saving treatment of peripheral atherosclerosis is also well documented.[5] Similarly, the recognition and timely management of patients with coronary thrombosis is well recognized as life-saving by both medical professionals and laypersons.

Why should the kidneys be different? The natural history of RAS is variable. But a significant fraction of patients with RAS have progressive narrowing of the inflow artery to the functioning renal mass. Using Doppler scan follow-up, Zierler et al[6] showed renal arteries with significant stenoses (>60%) have approximately a 20% progression of disease per year with 11% progressing to renal occlusion within 2 years. Similarly, using ultrasound scan to document renal size, Caps et al[7] showed progression to renal atrophy in patients with worsening RAS.

From the Division of Vascular Surgery,[a] University Hospitals Case Medical Center, Cleveland, Ohio; and the Department of Vascular Surgery,[b] University of Poitiers Medical Center, Poitiers, France.

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Reprint request: Vikram S. Kashyap, MD, University Hospitals Case Medical Center, 11100 Euclid Avenue, Cleveland, OH 44106-7060 (e-mail: vikram.kashyap@uhhospitals.org); and Jean-Baptiste Ricco, MD, PhD, University of Poitiers Medical School, Hospital Jean Bernard, Rue de la Milétrie, 86000, Poitiers, France (e-mail: jeanbaptistericco@gmail.com).

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It is estimated that chronic kidney disease affects 11% of the adult population in the United States with nearly 400,000 patients with end-stage renal failure. The morbidity and mortality of end-stage renal disease is staggering with US annual mortality rates of >20%.[8] Even lesser degrees of chronic kidney disease can have significant consequences as the risk of death increases as the glomerular filtration rate (GFR) falls.[9] Furthermore, reduced GFR is independently associated with the cardiovascular morbidity and hospitalization with severe renal impairment (GFR <30 mL/min/1.73 m^2). Despite the prevalence of chronic kidney disease, the relationship to RAS remains unclear. A significant fraction of patients on hemodialysis have renal vascular disease implicating that RAS may be an underappreciated component of renal failure.[10]

Myth #2. Patients with hypertension and renal artery stenosis have renovascular hypertension. One of the critical problems in assessing patients with RAS is the unclear relationship with concomitant hypertension. Goldblatt et al's[11] compelling studies helped the medical community understand the causal relationship of RAS to hypertension over 70 years ago. This led to several reports of curing hypertension by surgical revascularization a few years later. In pediatric or young adult populations with congenital or vasculitic causes of RAS, hypertension is closely aligned to the degree of unilateral RAS. With increasing unilateral stenosis, neurohormonal changes occur resulting in increased angiotensin II-induced blood pressure elevation. In older populations, essential (or primary) hypertension is rampant and appraising whether the RAS is a bystander or the culprit can be challenging for even the most experienced practitioner. A cavalier attitude by some is that in our current limitations of understanding this relationship, the only way to tell is the response after intervention. That is, treat everyone, help a few. Clearly, this position of "drive-by" stenting can lead to inappropriate use of technology, increased costs, and the real possibility of patient harm in cases of inadvertent renal injury.

Patients with severe hypertension with episodes of hypertensive crises seem to be the best candidates for RAS intervention.[12] The severity of hypertension may be seen as the need for increasing antihypertensive agents, increased dosage or frequency of medication, and sudden worsening in blood pressure control in an otherwise stable patient. Despite a plethora of studies to try to understand this relationship of RAS and hypertension, most studies (ie, renal vein renin sampling) are not sufficiently sensitive or specific to clearly implicate the RAS as the etiologic factor for the hypertension. A test with prognostic value in this arena will allow careful selection of patients that require intervention. Last, the current data on blood pressure reduction in trials are grossly estimated by the number of medications and/or reduction in dose as a surrogate to actual blood pressure measurements. The latter is a widely fluctuating physiological parameter[13] and deserves a more precise assessment.

Myth #3. Ischemic nephropathy is any patient with an escalating creatinine and bilateral renal artery stenosis. As opposed to unilateral RAS and resultant renovascular hypertension, bilateral RAS or stenosis in the artery leading to a single functioning kidney may lead to renal function loss. Renovascular hypertension may be overdiagnosed, but RAS causing renal insufficiency and eventual renal loss may be underappreciated and consequently undertreated.[10,14] This condition called "ischemic nephropathy" can be treated and leads to gratifying improvement in renal function. However, the tools to assess this in our current practice are the poorly sensitive serum creatinine (sCr), the GFR with calculations often based on sCr, and nuclear medicine testing where the images and interpretation can sometimes be challenging and lead to differences in subjective impression between observers.

Unfortunately, most patients with "ischemic nephropathy" presumably have renal function decline secondary to unrelated chronic renal disease from intrinsic renal glomerular loss secondary to a host of systemic processes. This may include inflammatory conditions and oxidative stress.[15]

Similar to myth #2, the likelihood of understanding in a particular patient whether renal function decline is due to RAS is often difficult. Many experienced practitioners have had the gratifying situation of observing rapid improvement in renal function after treating severe RAS to a single functioning kidney where the serum markers clearly delineate residual renal function. Likewise, the experience of patients with no improvement in their renal function despite a technically successful procedure is not uncommon. Salvage of the kidneys is best predicted by the downward slope of GFR or renal function before intervention.[16,17] Other prognostic modalities to identify renal mass retrieval may be novel magnetic resonance-based methods to understand the perfusion deficit in patients with ischemic nephropathy.[18] Novel technologies and assays would allow us to determine an infarcted renal mass from one that is ischemic, analogous to stress testing and biomarkers in the coronary beds.

Myth #4. Renal stenting is an easy procedure to do well. For the purposes of this debate, we are assuming intervention of the renal arteries means endovascular intervention. There is rich literature on the benefits of surgical revascularization of the renal arteries.[12,13] Surgical revascularization for retrieval of renal function can be accomplished with documented durable long-term results in centers of excellence with a dedicated interest in renovascular surgery.[19,20] However, this has largely been supplanted by endovascular means[21] because of the perceived lower initial morbidity of a purely percutaneous procedure as opposed to open revascularization in an elderly population with multiple comorbidities.

Technical advances have also spurred widespread adoption of endovascular treatment of RAS. Despite the rapid increase in renal stenting, trial data have documented the harm that can occur to the kidneys that we are trying to protect from deterioration. The kidney does not have the same discrete functional areas that would alert a clinician to

kidney decline after intervention other than where serious harm has occurred because of large emboli, renal infarction, dissection, reperfusion injury, or contrast-induced renal failure. Some of these may happen more than we realize. Some possible technical adjuncts that prevent these complications include adopting a 6Fr platform for intervention with the use of 0.014-inch guidewires and stent systems, rapid-exchange systems, using a distal protection device, using a "no touch" technique, anticoagulation/direct thrombin inhibition, and routine periprocedure double-antiplatelet therapy with aspirin and clopidogrel. Clearly, in other arterial beds, a distal protection device can be used to capture atheroembolic debris before reaching the end organ that we are trying to protect.[22] The use of a distal protection device during renal intervention makes intuitive sense given the capture of embolic debris in a significant fraction of cases.[23,24] Additional evidence that atheroembolic material that could cause renal parenchymal damage has been obtained via an ex vivo study using human arterial plaque specimens.[25] Currently, the outcome of renal percutaneous transluminal angioplasty and stenting with a distal protection device is being evaluated in the National Institutes of Health-supported randomized controlled Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial.[26]

Myth #5. The data from randomized trials are clear-cut. My debate opponent will try to convince you that multiple randomized controlled trials clearly show no benefit from renal artery stenting. One thing is clear: no benefit can be obtained in patients poorly selected for intervention. Another critical point: any benefit from an intervention can be negated by the poor performance of the procedure.

In the recent STAR publication, the investigators randomized 140 patients to medical therapy or renal artery stenting for atherosclerotic disease in the renal arteries at 10 European medical centers.[27] Patients were eligible for inclusion if creatinine clearance was <80 mL/minute per 1.73 m^2 and they had a 50% or greater stenosis. The primary endpoint was a 20% or greater fall in creatinine clearance. This occurred in 16% of the stent group and 22% of the medication group (P = NS). The authors concluded that stent placement had no clear benefit on preventing renal function decline in this small study. Of note, only 46 of the 64 patients assigned to stenting actually had a stent placed. Of great concern was that 12 of the 64 patients (19%) did not get a stent because they had <50% stenosis at the time of angiography despite the preoperative imaging (computed tomographic angiography, magnetic resonance angiography) indicating a high-grade stenosis. One can assume that the medical therapy group also had a large fraction of patients with insignificant and benign RAS (<50%). The rates of complications in the stented group, including two procedure-related deaths, one death from an infected hematoma, one renal failure after kidney cholesterol embolism, two technical failures, and 10 femoral hematomas, paint a troubling picture in a group of 46 renal stent procedures.

Angioplasty and Stent for Renal Artery Lesions is an international, multicenter trial that enrolled 806 patients and randomized them to intervention or medical management.[28] The primary outcome was again renal function measured as a reciprocal of the sCr level. The two groups had similar rates of renal events, cardiovascular events, and death, as will be outlined by our debate opponent. But, this trial has many limitations. Of greatest concern were the inclusion criteria of patients into the trial. Patients were eligible for enrollment if they had atherosclerotic disease in the renal arteries and were considered suitable for endovascular revascularization. However, only 59% of enrolled patients had an RAS >70% with essentially the remainder having 50% to 70% stenoses. Physicians did not enroll patients if they thought that renal revascularization would be beneficial—the exact target that any randomized controlled trials in this arena should focus on. Thus, the patients that we assume would have the greatest benefit from revascularization were excluded. Neither the medical management nor the intervention techniques were standardized and there was no core laboratory to review the images and corroborate the renal artery stenoses treated. In fact, often the severity of the stenosis is overestimated by the interventionalist when compared to the core laboratory's nonbiased assessment.[29] Thus, many of these patients may have actually had modest (ie, 50%) stenoses, rather than critical stenoses to the kidney they were trying to protect. Seventeen percent of patients did not undergo intervention after angiography because the severity of RAS by noninvasive methods was not confirmed on angiography; one can assume a similar proportion of low-profile lesions in the medical group. Additionally, 40% of enrollees had sCr levels <150 μmol/L (<1.7 mg/dL), with a large fraction of these patients with normal creatinine and only on an average 2.8 antihypertensive agents. What was the indication for treatment in these patients? In the 359 patients that actually underwent revascularization, 31 patients (9%) had complications. This included renal embolization,[5] renal artery occlusion,[4] renal artery perforation,[4] femoral artery aneurysm,[1] and cholesterol embolization[3] leading to gangrene and amputation. With any revascularization procedure for atherosclerosis, we are trying to "beat" the natural history of the disease. Patients that have high-grade renal artery lesions, rapidly falling GFR, and stenoses to the whole renal mass (ie, bilateral renal stenoses, stenosis to a single-functioning kidney) may benefit from renal stenting. But, trials that enroll large fractions of the patients with benign lesions and then have high complication rates cannot be expected to be successful.

CONCLUSIONS

With the current data available, one may not be able to conclude that "vast majority of patients with renal artery stenoses require intervention," the provocative position assigned to this author. On the other hand, the position "the vast majority of patients with renal artery stenoses do not require intervention" leaves many patients without an option that may be kidney- and life-saving. We all agree that

more research is needed in this area. One day, clinicians will be able to discern that a particular RAS is the culprit that leads the kidney end organ to cause hypertension and/or become ischemic and atrophy. In the interval, careful evaluation of patients with RAS and renal insufficiency by a collaborative team of nephrologists and vascular specialists seems to be warranted. This may offer patients the best opportunity for long-term renal salvage and survival, whether it be medical treatment or intervention.

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PART II: THE VAST MAJORITY OF PATIENTS WITH ATHEROSCLEROTIC RENAL ARTERY STENOSES DO NOT REQUIRE INTERVENTION

Fabrice Schneider, MD, and Jean-Baptiste Ricco, MD, PhD, *Poitiers, France*

Introduction. The rate of percutaneous renal artery intervention among Medicare beneficiaries increased 2.4-fold in 2000 as compared with 1996 on the premise that associated hypertension and renal function would be cured.[1] To date, however, recent randomized controlled trials (RCTs) on primary stenting for atherosclerotic renal artery stenosis (ARAS) are not supporting evidence for its use.[2] The goal of this debate was to summarize the evidence on percutaneous renal artery stenting for ARAS.

THE CLINICAL PROBLEM

The reported incidence of ARAS in the Medicare population is 0.5% overall,[3] but as these patients are often asymptomatic, the true frequency of ARAS is probably higher. ARAS is associated with hypertension, chronic kidney disease, and cardiac disorders, although it is not clear whether these associations are causal.[4] Nevertheless, patients with ARAS after adjustment for other traditional risk factors, are at increased risk for cardiovascular events with a risk of coronary event that is increased by a factor of two and markedly decreased survival.[5] These outcomes are rare

in patients with ARAS that are treated medically[6] and probably related to distribution and severity of atherosclerosis in other vascular beds.[7,8]

EVALUATION

ARAS is suspected in patients with the onset of hypertension after 50 years of age. Confirmation of the diagnosis is made by imaging. Doppler scan measurement of renal artery velocity provides an assessment of the severity of the stenosis. Alternative methods include magnetic resonance angiography, computed tomographic angiography, and digital subtraction angiography with the use of small catheters and limited amounts of contrast media. All these tests are useful in confirming the diagnosis of ARAS, but Drieghe et al[9] have shown that even if renal angiography and color duplex ultrasound scans correlate well, both approaches tend to overestimate the ARAS severity when compared with the measured trans-stenotic pressure gradient using 0.014 pressure wires. Again, none of these techniques can establish the functional significance of ARAS. Even the documentation of a trans-stenotic pressure gradient in ARAS does not necessarily mean that the given stenosis is the cause of hypertension.

Risk factors and medical treatment. A major confounder related to the treatment of ARAS is competing risk from other manifestations of atherosclerosis, including stroke, acute coronary syndrome, and congestive heart failure. The risk of these events is greater than the risk of complications related specifically to ARAS. They reflect widespread atherosclerotic disease elsewhere.[10] In this context, medical therapy remains the cornerstone of treatment for ARAS. Multi-drug regimens are needed for blood pressure control, including a renin-angiotensin-aldosterone inhibitor, alpha or beta-blocker, diuretic, and calcium channel antagonist. The demonstrated benefits of antiplatelet therapy and statins in patients with atherosclerotic disease also provide support for their use in patients with ARAS.

PROSPECTIVE RANDOMIZED CONTROLLED TRIALS

Benefit of renal stenting over angioplasty alone. Primary stenting of ARAS was compared to angioplasty alone in one small RCT.[11] The results of this trial were comparable with those of a meta-analysis that compared these two techniques.[12] There was a 65% reduction in risk of restenosis with stents at 6-month angiography, but there was no difference in blood pressure or renal outcome. Primary stenting thus showed a more favorable outcome with fewer reinterventions than angioplasty for ARAS.[13]

Benefit of renal artery stenting vs surgery. Only one RCT compared renal artery stenting vs open surgical revascularization in patients with ARAS.[14] Inclusion criteria were severe hypertension and ARAS >70%. There was no significant difference in treatment outcome (ie, blood pressure, renal outcome, midterm patency, and complications). But as surgery was associated with a longer duration of hospitalization (18 days vs 10 days), the authors suggest that renal artery stenting should be preferred to surgery in patients who do not need concomitant aortic revascularization.

In addition to this RCT, a large meta-analysis[15] comparing the outcome of open surgical revascularization vs endovascular treatment showed that endovascular patency declined by 0.26% per month and that open revascularization showed greater improvement for hypertension by 21% (95% confidence interval [CI], 9%-33%; $P = .001$) and for renal function by 34% (95% CI, 18%-54%; $P = .001$) but with a higher surgical mortality, 3.1% (95% CI, 1.8%-4.4%; $P = .01$) that became insignificant when concomitant aortic surgery was excluded. Despite the advantages of open revascularization, the attendant morbidity and mortality of surgery ensures a significant role for renal artery stenting in most patients. However, there will continue to be a role for open renal artery revascularization in young patients with severe RAS who are more likely to benefit from the durability of renal bypasses.

Comparison of renal artery stenting with medical treatment alone. Comparison of renal artery stenting plus medical treatment with medical treatment alone was available in three RCTs (Table I). Two RCTs of limited power[16,17] compared stent placement with medical treatment in patients with ARAS with severe hypertension or recent impairment of renal function. These two studies did not show any significant improvement in renal function, blood pressure outcome, or survival in patients with renal stenting as compared with medical treatment alone.

A larger trial, Angioplasty and Stenting for Renal Artery Lesions (ASTRAL) further questions the benefit of ARAS stenting vs medical therapy alone.[18] This RCT involved 806 patients with ARAS. Patients were enrolled if clinical findings (recent onset of hypertension or unexplained decreasing renal function) suggested a diagnosis of ARAS confirmed by duplex echography, computed tomographic angiography, or magnetic resonance angiography in at least one renal artery and if the physician was uncertain that the patient would benefit from revascularization. ARAS severity was between 50% and 70% diameter-reducing lesion in 40% of the patients enrolled in the trial and exceeded 70% in 60% of them. After 5 years, change in renal function, mean systolic arterial pressure, and number of cardiovascular events or death did not differ significantly between the two groups. This result was confirmed in a subgroup of patients with high-grade or bilateral ARAS. Among patients with renal artery stenting, 4.2% suffered procedure-related major complications, including renal artery rupture, dissection, thrombosis, embolization, and worsening of renal insufficiency (Table I). The ASTRAL study concluded that there was no advantage of revascularization as compared with medical treatment in patients with ARAS.

This trial was criticized because of its enrollment strategy excluding patients who would likely benefit more from renal stenting. In addition, 40% of patients with renal artery stenting had moderate RAS between 50% and 70% diameter-reducing lesions, for which only limited benefit from revascularization could be expected. Pressure gradient across the

Table I. Randomized controlled trials comparing renal artery stenting with medical therapy alone for atherosclerotic renal artery stenosis

References	*No. of patients*	*Inclusion criteria*	*Renal artery stenosis*	*Renal function*	*Follow-up (mos)*	*Outcomes*
Ziakka et al[16]	36 with stents 46 with MT	Hypertension	74% (mean)	SCr: 2.3 mg/dL	48	Renal function improved or stabilized in 64% of patients with stents vs 70% with medication alone (NS). Hypertension cured or improved in 78% of patients with stents vs 71.4% in the medical group (NS).
Bax et al[17]	64 with stents 76 with MT	Impaired renal function	≥50%	Creatinine clearance <80 mL/minute/1.73 m^2	24	No difference in renal event-free survival (HR, 0.73; 95% CI, 0.33-1.61). Procedure-related major complications: -2 procedure-related deaths (3%) -1 late death due to an infected hematoma -1 patient requested dialysis secondary to cholesterol embolism
Wheatley et al[18]	403 with stents 403 with MT	Uncontrolled hypertension or unexplained impaired renal function	>50%	GFR: 40 mL/minutes/ 1.73 m^2	34	No difference in renal event-free survival, GFR decline rate, blood pressure, cardiovascular events, and survival. Procedure-related major complications (n = 17, 4.2%): -5 kidney embolisms -4 renal artery occlusions -4 renal artery perforations -1 renal artery aneurysm -3 peripheral embolisms (amputations)

CI, Confidence interval; *GFR,* glomerular filtration rate; *HR,* hazard ratio; *MT,* medical treatment alone; *NS,* not significant; *sCr,* serum creatinine.

stenosis was not measured in this study and there was no core laboratory to validate the on-site visual estimates of ARAS. There were also significant crossovers in this study with only 359 of 403 patients randomized to renal artery stenting who underwent the procedure, whereas 24 of 403 patients assigned to medical treatment underwent intervention. But when examined on a per-protocol analysis, there was still no apparent benefit for renal artery stenting.

Randomized controlled trials: What have we learned? The results of these three RCTs need to be considered carefully in light of their design. The enrollment strategy of the ASTRAL trial regarding the doubt of the effectiveness of revascularization meant that clinicians were uncertain as to whether they should intervene; consequently, they considered the randomization to be appropriate. Despite some criticisms, almost all patients enrolled in these RCTs would have been considered for renal artery stenting in normal clinical practice. In the ASTRAL trial, the skills of the physicians performing renal stenting were not formally assessed, but their expertise was reflected in a technical success rate of 95% and the rate of serious complications was similar to that of other methodologically solid studies with rigorous record-keeping. In summary, these trials provide evidence that, in typical patients considered for renal revascularization in today's current clinical practice, intervention offers no clinical benefit and has some risk as compared to best medical treatment alone. It is possible, however, that renal artery stenting might benefit a minority of patients with specific clinical presentations that were not specifically addressed in these RCTs.

Ongoing trials. Following the ASTRAL study, three ongoing RCTs were designed to better assess renal and cardiac outcomes after renal artery stenting. The Renal Atherosclerotic Revascularization study compares renal

Table II. Reasons for skepticism regarding renal artery stenting

1. Failure to define causal role of ARAS in disease syndromes such as hypertension or worsened renal function.
2. Imprecise definition of ARAS with inclusion of subcritical ARAS in trials and lack of methods to assess renal hemodynamics.
3. Compensatory action of the nonstenotic kidney.
4. Advances in medical management: blockade of the renin-angiotensin system, effective antihypertensive drugs, antiplatelet agents and statins.
5. Complications of ARAS stenting: kidney embolism, occlusion, perforation or dissection of the renal artery, contrast nephropathy.
6. Negative outcomes from randomized controlled trials.

ARAS, Atherosclerotic renal artery stenosis.

stenting with best medical treatment alone with a composite endpoint that includes death, dialysis, and doubling of serum creatinine.[19] The RADAR study compares best medical treatment with best medical treatment plus renal artery stenting in patients with hemodynamically relevant atherosclerotic RAS. The primary endpoint being the change in estimated glomerular filtration rate between the two groups during 12-month follow-up. Secondary endpoints included technical success, change in average blood pressure, and in left ventricular mass index. Finally, the Cardiovascular Outcomes with Renal Atherosclerotic Lesions trial[20] compares best medical treatment alone with renal stenting on a composite heart, and vascular and renal endpoint. In this trial, angiography and transluminal pressure gradients were used to determine entry in the study with a core laboratory using quantitative analysis. Patients with a gradient ≥20 mm Hg and a renal artery >35 mm in diameter were considered for randomization.

Technical issues related to atherosclerotic renal artery stenosis stenting. Renal artery stenting has improved over recent years with small-platform, including a less traumatic premounted low-profile stent on 0.014- or 0.018-inch wire, less traumatic 2.5 to 4Fr shaft balloons, steerable catheters, smaller puncture site, and rapid-exchange systems avoiding the need for long wires. Despite these significant improvements, ARAS stenting is not an easy procedure and atheroembolic disease remains a major concern with manipulation of the renal artery, which is a predictor of embolic events.[21] Distal embolic protection devices have been logically used to avoid this complication. But in an RCT, Cooper et al[22] showed a decline in estimated glomerular filtration rate in both groups of patients with and without protection device. In this series, the only group with no loss of glomerular filtration was receiving both the embolic protection device and a platelet glycoprotein inhibitor (abciximab) suggesting a risk of intra-arterial thrombosis triggered by the use of the embolic protection device.

Refining the approach to renal artery revascularization. As renal artery stenting falls short in these RCTs, many nephrologists have moved toward a more conservative approach concerning ARAS (Table II) probably also to counterbalance the attitude of aggressive cardiologists and radiologists.[23] Despite the difficulty in demonstrating benefits of renal artery stenting in large groups that included heterogeneous populations with a mixture of high- and low-risk patients, pathophysiological rationale and the positive results of some small series have provided valid arguments for renal stenting in a few patients with ARAS with deteriorating renal function after receiving angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers and in patients with flash edema or uncontrolled heart failure.[24,25] In addition, many physicians recognize that some patients with severe stenosis particularly affecting both renal arteries or a solitary kidney should be considered as potential candidates for renal artery stenting[26] even if the ASTRAL study showed no difference in outcome between renal artery lesions of varying severity.

CONCLUSIONS

Recent evidence shows that optimal medical treatment, including statins and risk reduction factors should be the preferred option for most patients with ARAS. It is almost certain that the vast majority of typical patients now being subjected to renal artery stenting show no added benefits regarding blood pressure and kidney function as compared to best medical treatment alone. But it is equally important to recognize that a minority of patients with rapidly progressive hypertension or renal insufficiency and flash pulmonary edema, or with specific lesions such as bilateral severe renal artery stenosis, or solitary kidney, do have a benefit from restoring kidney perfusion.

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EDITORS' COMMENTARY

Thomas L. Forbes, MD, and **Jean-Baptiste Ricco, MD, PhD,** *London, Ontario, Canada; and Poitiers, France*

It was expected that information resulting from recently completed randomized controlled trials would clarify the role of renal artery interventions in patients with atherosclerotic renal artery stenoses. Unfortunately, in this respect, we were left disappointed. Concerns regarding such issues as inclusion criteria limited the validity of these studies' conclusions, leaving a persistent knowledge gap into which our debaters step.

Although the authors were given separate charges, their conclusions are more similar than different. They both recognize the need for further study and information to elucidate the role of renal artery interventions. They recognize that we currently cannot accurately predict the natural history of any individual renal artery lesion, nor recognize entirely which lesions are responsible for a patient's hypertension or renal insufficiency. So instead of recommending whether the majority or the minority of patients should be intervened upon, they appropriately meet somewhere in the middle.

With the present uncertainty, the authors propose a multidisciplinary, collaborative approach to these often complicated clinical situations to arrive at decisions regarding individual patients. They propose a more aggressive approach in patients with specific criteria, including progressive hypertension, renal insufficiency with flash pulmonary edema, bilateral severe renal artery stenoses, and stenoses with a solitary kidney. Until further information is hopefully obtained from ongoing trials, this selective approach seems reasonable and most prudent.